UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Aflibercept Products Utilization Management Medical Policy
- Eylea® (aflibercept intravitreal injection – Regeneron)
- Eylea® HD (aflibercept intravitreal injection – Regeneron)
- Pavblu™ (aflibercept-ayyh intravitreal injection – Amgen)

REVIEW DATE: 10/30/2024

OVERVIEW

Aflibercept is a vascular endothelial growth factor (VEGF) inhibitor.[1-3] Ophthalmic aflibercept products, Eylea, Eylea HD, and Pavblu, are given intravitreally for the treatment of ophthalmic conditions. Pavblu is a biosimilar to Eylea.[3]

Eylea and Pavblu are indicated for the following uses:[1-3]
- **Diabetic macular edema**.
- **Diabetic retinopathy**.
- **Macular edema following retinal vein occlusion**.
- **Neovascular (wet) age-related macular degeneration**.

Eylea is also indicated for the treatment of **retinopathy of prematurity**.[1]

Eylea HD, a high dose aflibercept product, is indicated for the following uses:[6]
- **Diabetic macular edema**.
- **Diabetic retinopathy**.
- **Neovascular (wet) age-related macular degeneration**.

Dosing Information:

The recommended dosing for Eylea and Pavblu for each indication is as follows:
- Diabetic macular edema or Diabetic retinopathy: 2 mg via intravitreal injection once every 4 weeks (approximately every 28 days, monthly) for the first five injections, followed by 2 mg once every 8 weeks (2 months). Although Eylea/Pavblu may be dosed as frequently as 2 mg every 4 weeks (approximately every 25 days, monthly), additional efficacy was not demonstrated in most patients when Eylea/Pavblu was dosed every 4 weeks compared to every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 20 weeks (5 months).
- Macular edema following retinal vein occlusion: 2 mg via intravitreal injection once every 4 weeks (approximately every 25 days, monthly).
- Neovascular (wet) age-related macular degeneration: 2 mg via intravitreal injection every 4 weeks (approximately every 28 days, monthly) for the first 12 weeks (3 months), followed by 2 mg every 8 weeks (2 months). Although Eylea/Pavblu may be dosed as frequently as 2 mg every 4 weeks (approximately every 25 days, monthly), additional efficacy was not demonstrated in most patients when Eylea/Pavblu was dosed every 4 weeks compared with every 8 weeks. Some patients may need every 4 week (monthly) dosing after the first 12 weeks (3 months). Although not as effective as the recommended every 8 week dosing regimen, patients may also be treated with one dose every 12 weeks after one year of effective therapy.
- Retinopathy of prematurity (Eylea only): 0.4 mg via intravitreal injection. Treatment is initiated with a single injection per eligible eye and may be given bilaterally on the same day. Injections

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may be repeated in each eye; treatment interval between doses injected into the same eye should be at least 10 days.

The recommended dosing for Eylea HD for each indication is as follows:

- Diabetic macular edema: 8 mg via intravitreal injection every 4 weeks (approximately every 28 days, +/- 7 days) for the first three doses, followed by 8 mg once every 8 to 16 weeks, +/- 1 week.
- Diabetic retinopathy: 8 mg via intravitreal injection every 4 weeks (approximately every 28 days, +/- 7 days) for the first three doses, followed by 8 mg once every 8 to 12 weeks, +/- 1 week.
- Neovascular (wet) age-related macular degeneration: 8 mg via intravitreal injection every 4 weeks (approximately every 28 days, +/- 7 days) for the first three doses, followed by 8 mg once every 8 to 16 weeks, +/- 1 week.

Other Uses with Supportive Evidence for Eylea and Pavblu

Overproduction of VEGF may lead to other eye conditions, including neovascular glaucoma and other retinal and choroidal neovascular conditions affecting the eye.[4,5] The VEGF inhibitors have the potential to be used off-label to reduce or slow visual impairment or vision loss associated with other eye conditions related to increased VEGF production.[4,6,7] The use of VEGF inhibitors have been shown to stop the angiogenic process, maintain visual acuity, and improve vision in patients with certain neovascular ophthalmic conditions. Therefore, research is rapidly evolving on the use of VEGF inhibitors in other neovascular ophthalmic conditions that threaten vision.[6,7]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of the intravitreal aflibercept products (Eylea, Eylea HD, and Pavblu). Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with the intravitreal aflibercept products as well as the monitoring required for adverse events and long-term efficacy, approval requires the intravitreal aflibercept products to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

I. Coverage of Eylea and Pavblu is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Diabetic Macular Edema. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Dosing. Approve if the dose meets BOTH of the following (A and B):
A) The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 25 days for each eye being treated.

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2. Diabetic Retinopathy. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Dosing. Approve if the dose meets BOTH of the following (A and B):
A) The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 25 days for each eye being treated.

3. Macular Edema Following Retinal Vein Occlusion. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Dosing. Approve if the dose meets BOTH of the following (A and B):
A) The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 25 days for each eye being treated.

4. Neovascular (Wet) Age-Related Macular Degeneration. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Dosing. Approve if the dose meets BOTH of the following (A and B):
A) The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 25 days for each eye being treated.

5. Retinopathy of Prematurity. Approve for 1 year if administered by or under the supervision of an ophthalmologist.

Dosing. Approve if the dose meets BOTH of the following (A and B):
A) The dose is 0.4 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 10 days for each eye being treated.

Other Uses with Supportive Evidence

6. Other Neovascular Diseases of the Eye. Approve for 1 year if administered by or under the supervision of an ophthalmologist.
Note: Examples of other neovascular diseases of the eye include neovascular glaucoma, sickle cell neovascularization, and choroidal neovascular conditions.

Dosing. Approve if the dose meets BOTH of the following (A and B):
A) The dose is 2 mg administered by intravitreal injection for each eye being treated; AND
B) The dosing interval is not more frequent than once every 25 days for each eye being treated.

II. Coverage of Eylea HD is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. **Diabetic Macular Edema.** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   A) The dose is 8 mg administered by intravitreal injection for each eye being treated; AND
   B) The dosing interval is not more frequent than once every 21 days for three doses, followed by not more frequent than once every 7 weeks for each eye being treated.
   Note: The recommended dose is once every 4 weeks (approximately every 28 days +/- 7 day) for the first three doses, followed by one dose every 8 to 16 weeks, +/- 1 week.

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2. **Diabetic Retinopathy.** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   A) The dose is 8 mg administered by intravitreal injection for each eye being treated; AND
   B) The dosing interval is not more frequent than once every 21 days for three doses, followed by not more frequent than once every 7 weeks for each eye being treated.
   Note: The recommended dose is once every 4 weeks (approximately every 28 days +/- 7 day) for the first three doses, followed by one dose every 8 to 12 weeks, +/- 1 week.

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3. **Neovascular (Wet) Age-Related Macular Degeneration.** Approve for 1 year if administered by or under the supervision of an ophthalmologist.

   Dosing. Approve if the dose meets BOTH of the following (A and B):
   A) The dose is 8 mg administered by intravitreal injection for each eye being treated; AND
   B) The dosing interval is not more frequent than once every 21 days for three doses, followed by not more frequent than once every 7 weeks for each eye being treated.
   Note: The recommended dose is once every 4 weeks (approximately every 28 days +/- 7 day) for the first three doses, followed by one dose every 8 to 16 weeks, +/- 1 week.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of the intravitreal aflibercept products is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Eylea® intravitreal injection [prescribing information]. Tarrytown, NY: Regeneron; December 2023.
2. Eylea® HD intravitreal injection [prescribing information]. Tarrytown, NY: Regeneron; December 2023.
3. Pavblu™ intravitreal injection [prescribing information]. Thousand Oaks, CA: Amgen; August 2024.
4. Barakat MR, Kaiser PK. VEGF inhibitors for the treatment of neovascular age-related macular degeneration. *Expert Opin Investig Drugs*. 2009;18(5):637-646.
5. Tolentino M. Systemic and ocular safety of intravitreal anti-VEGF therapies for ocular neovascular disease. *Surv Ophthalmol*. 2011;56(2):95-113.
6. Kinnunen K, Ylä-Herttuala S. Vascular endothelial growth factors in retinal and choroidal neovascular diseases. *Ann Med*. 2012;44(1):1-17.

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7. Horsley MB, Kahook MY. Anti-VEGF therapy for glaucoma. *Curr Opin Ophthalmol*. 2010;21(2):112-117.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/15/2023
Annual Revision	**Pavblu:** Pavblu (biosimilar to Eylea) was added to the policy; conditions and criteria for approval for Pavblu are identical to those for Eylea. **Policy name:** Policy name was changed from Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Eylea and Eylea HD to Ophthalmology – Vascular Endothelial Growth Factor Inhibitors – Aflibercept Products.	10/30/2024

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